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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.

EXAMINER

ART UNIT	PAPER NUMBER
	C1

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/526,320	Applicant(s) GABRILOVICH ET AL.
	Examiner Anne M Beckerleg	Art Unit 1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 August 2001*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-60* is/are pending in the application.

4a) Of the above claim(s) *5-10 and 38-60* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 11-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4*.
4)☐ Interview Summary (PTO-413) Paper No(s). _____.
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other:

Applicant's response to the restriction/election received on 8/22/01 has been entered. Applicant's election without traverse of Group I, claims 1-37, is acknowledged. Applicant's further election of the species tumor suppressor genes is also acknowledged. Claims 5-10 and 38-60 are therefore withdrawn as being drawn to subject matter non-elected without traverse in paper no. 7. Claims 1-4 and 11-37 are currently under examination in the instant application. An action on the merits follows.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4, and 11-37 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of inhibiting tumor growth of a p53 positive tumor capable of processing and presenting p53 epitopes in the context of MHC on the tumor cell surface comprising intradermal administration of a plasmid DNA encoding p53 or a replication defective adenovirus encoding p53, does not reasonably provide enablement for treating any type of hyperproliferative disease comprising the intradermal administration of any type of expression construct encoding any tumor suppressor gene. The specification does not enable any person

skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The specification discloses the administration of recombinant expression constructs encoding wild-type or mutant p53 wherein the expression of p53 in dendritic cells in vivo results in the generation of p53 specific CTL responses capable of having a therapeutic effect on a p53 expressing tumor. The specification provides several working examples of the instant invention which are limited to the administration of splenic or bone-marrow derived dendritic cells transduced ex vivo with an adenoviral vector encoding p53 under control of the CMV I/E promoter to mice. The working examples demonstrate that the intravenous, subcutaneous, or intraperitoneal injection of in vitro transduced DCs with adenovirus p53 results in the generation of p53 specific CTL, and in the case of mice which received intravenous administration of the transduced DCs, inhibition of growth of a p53 positive tumor. It is noted that the specification does not provide any working examples which utilize intradermal injection, or which involve the direct injection of any type of expression construct encoding p53 or any other tumor suppressor gene.

The specification does not provide an enabling disclosure for the treatment of any hyperproliferative disease comprising the direct intradermal administration of any expression construct encoding any tumor suppressor gene including p53. The specification discloses the treatment of many types of "hyperproliferative" diseases which include autoimmune diseases, cancer, and vascular degenerative diseases such as restenosis. While the specification discloses

that mutations and alterations in various tumor suppressor genes are associated with tumorigenesis, the specification does not establish a role for any tumor suppressor gene in the development or etiology of any autoimmune disease including RA or IBD, or for restenosis. Further, the art at the time of filing does not teach that the overexpression of p53 or any other tumor suppressor gene is associated with any disease except cancer. As discussed in the previous paragraph, the specification also does not provide any working examples involving the direct administration of any expression construct encoding any tumor suppressor gene or demonstrate that immune responses generated against p53 have any effect on any hyperproliferative disease other than cancer. In the absence of evidence to the contrary, the skilled artisan would not have been able to predict whether p53 or any other tumor suppressor gene is in fact associated with any hyperproliferative disease other than cancer, or whether a CTL or antibody response could in fact be generated against any tumor suppressor gene which would correlate with a therapeutic effect on the hyperproliferative disease. Thus, based on the known functions and disease associations for the disclosed tumor suppressor genes, the lack of guidance provided by the specification for hyperproliferative diseases other than cancer which are associated with alterations or overexpression of p53 or any other tumor suppressor gene, and the breadth of the claims, it would have required undue experimentation to practice the invention as claimed for any hyperproliferative disease other than cancer.

The specification does not provide an enabling disclosure for the treatment of any cancer comprising the direct intradermal administration of any tumor suppressor gene. The regulation of

cell growth is a complex process involving numerous inter- and intracellular interactions. Disregulation of this process through genetic mutation results in neoplasia. As Vogelstein et al. explains, " each individual cancer arises not from a single mutation, but from the accumulation of several mutations" (Vogelstein et al. (1993) Trends in Genetics, Vol. 9(4), page 138, lines 9-11). A corollary to this principle is that each type of tumor, lung versus colon, versus lymphoid, may have different sets of mutations. In general, two major categories of mutations can be found in transformed cells, mutations in tumor suppressor genes, and mutations in oncogenes. Vogelstein et al. teach that while the mutation of the abl oncogene to c-abl can be found in many chronic myelogenous leukemias, mutations in the tumor suppressor gene APC are more common in colorectal tumors (Vogelstein et al. (1993) Trends in Genetics, Vol. 9(4), page 140, column 2, paragraphs 2-3, and page 141, column 1, paragraphs 1-2). In addition, individual transformed cells of a tumor acquire new mutations over time, resulting in clonal subsets with differential sensitivities to drugs, radiation, and immune attack (Vogelstein et al. (1993) Trends in Genetics, Vol. 9(4), page 141, column 1, paragraph 1). Thus, successful use of the instant invention for the treatment of a particular tumor by administration of a wild type tumor suppressor gene would require detailed knowledge of the genetic mutations of a particular type of tumor in order to insure that any immune responses generated against the vector expressed tumor suppressor gene would recognize the target tumor cell. In addition, cancer immunotherapy using tumor antigens is further complicated by the fact that in order for the tumor antigen specific T cells to be effective against the tumor, the tumor must be able to express recognizable levels of peptide/MHC class I

complexes derived from tumor antigen. At the time of filing, the art teaches that tumors evade immune responses by a variety of mechanisms including down-regulation of TAP and MHC-encoded proteasome components, loss of antigenic epitopes by either lack of expression or mutations, loss of functional β_2m expression , and loss of particular MHC class I alleles (Restifo et al (1993) J. Immunother., Vol. 14, page 183, col 1, lines 8-14, and page 184, col. 2). The loss or mutation of any of these molecules would prevent the tumor cells from being recognized by the tumor specific cytotoxic T cells. The applicant's working examples, as discussed above, are limited to the generation of anti-p53 immune responses to tumor which overexpress p53 and are capable of presenting p53 peptides for recognition by anti-p53 CTL. The specification does not provide sufficient guidance or evidence that anti-p53 immune responses are capable of having a therapeutic effect on a tumor which either does not express p53, or which is incapable of presenting p53 peptide epitopes for recognition by helper or cytotoxic T cells. Therefore, in view of the heterogeneity of tumor suppressor and oncogene mutations in a particular tumor cell, the various mechanisms by which tumor cells evade immune responses, the lack of guidance provided by the specification for the treatment of p53 negative or immune resistant tumor cells, and the breadth of the claims, the skilled artisan would have considered it unpredictable at the time of filing to treat any type of tumor by generating anti-p53 immune responses according to the instant methodology other than a tumor which overexpresses p53 and which is capable of presenting p53 epitopes for T cell recognition.

The specification does not provide an enabling disclosure for the treatment of any p53 overexpressing tumor comprising the intradermal administration of any expression construct encoding p53 other than a naked plasmid DNA encoding p53 or a replication defective adenovirus encoding p53. As noted above, the specification's working examples are limited to experiments involving the administration of dendritic cells transduced ex vivo with an adenovirus encoding p53. The specification does not provide any specific evidence that therapeutic levels of anti-p53 CTL can be generated by the direct intradermal administration of any expression construct encoding p53. At the time of filing, Hurpin et al. teaches the route of vector delivery has a significant effect on the generation of immune responses to a tumor suppressor gene such as p53, and that successful routes of administration vary between different vector systems. In particular, Hurpin et al. teaches that while intradermal injection of a plasmid encoding p53 in mice results in the generation of therapeutic levels of anti-p53 CTL capable of inhibiting p53 expressing tumor growth, the intradermal injection of a vaccinia virus encoding p53 is completely ineffective in generating either anti-53 antibodies or CTL, and does not protect against p53 tumor challenge (Hurpin et al. (1998) Vaccine, Vol. 16, No. 2/3, 208-215, see page 211, Figure 1). The art at the time of filing also teaches the high level of unpredictability of generating therapeutic levels of gene expression using currently available expression vectors. Verma et al. states that, "[t]he Achilles heel of gene therapy is gene delivery..", and that, "most of the approaches suffer from poor efficiency of delivery and transient expression of the gene" (Verma et al. (1997) Science, Vol. 389, page 239, column 3, paragraph 2). Marshall concurs, stating that, " difficulties in getting

genes transferred efficiently to target cells- and getting them expressed- remain a nagging problem for the entire field", and that, "many problems must be solved before gene therapy will be useful for more than the rare application" (Marshall (1995) Science, Vol. 269, page 1054, column 3, paragraph 2, and page 1055, column 1). Orkin et al. further states in a report to the NIH that, " .. none of the available vector systems is entirely satisfactory, and many of the perceived advantages of vector systems have not been experimentally validated", and that," [w]hile the expectations and the promise of gene therapy are great, clinical efficacy has not been definitively demonstrated at this time in any gene therapy protocol" (Orkin et al. (1995) "Report and recommendations of the panel to assess the NIH investment in research on gene therapy", page 1, paragraph 3, and page 8, paragraph 2). Among the many factors that the art teaches affect efficient gene delivery and sustained gene expression are anti-viral immune responses, and the need for appropriate vector/promoter combinations for a particular cell type. In regards to the latter issue, Verma states that, "the search for such combinations is a case of trail and error for a given cell type" (Verma, (1997) Nature, 389, page 240). Thus, in view of the art recognized unpredictability of generating therapeutic levels of gene expression using both viral and non-viral vectors at the time of filing, the art recognized differences in the ability of vectors to generate immune responses to encoded proteins based on the route of administration, the specific teachings of Hurpin et al. that the intradermal injection of vaccinia virus encoding p53 fails to generate p53 immune responses, the lack of working examples demonstrating the direct administration of any expression construct

encoding p53 using any route of administration, and the breadth of the claims, it would have required undue experimentation to practice the scope of the invention as claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 11, 20-30, and 33 are rejected under 102(b) as being anticipated by Hurpin et al. (1998) Vaccine, Vol. 16, No. 2/3, 208-215. The applicant claims methods of treating a hyperproliferative disease in a subject by identifying a subject with a hyperproliferative disease characterized by alteration or increased expression of a self gene product and intradermally administering an expression construct comprising a self tumor suppressor gene under control of a promoter operable in eukaryotic dendritic cells. The applicant further claims said methods wherein the hyperproliferative disease is a cancer selected from a group which includes breast cancer, wherein said tumor suppressor gene is p53, and wherein said promoter is the CMV IE promoter. In addition, the claims recite said methods wherein the immune response generated against p53 is a CTL response.

Hurpin et al. teaches that the intradermal injection of a plasmid encoding wild type p53 results in the generation of p53 specific CTL and protection from the growth of a p53 overexpressing mastocytoma (Hurpin et al., page 212, Figure 3, and page 213, Figure 4). Hurpin et al. further teaches that the plasmid encodes p53 under transcriptional control of the CMV immediate-early promoter, and that the plasmid was administered intradermally at five separate sites on the back (Hurpin et al., page 209, column 1, paragraph 3, and column 2, paragraph 2). Hurpin et al. also teaches that more than 50% of tumors overexpress p53 and further teaches that overexpression of p53 can be determined using well known techniques in molecular biology (Hurpin et al., page 1, column 2, paragraph 2, and page 209). Thus, by teaching all the elements of the claims, Hurpin et al. anticipates the instant invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to

the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 12-19 and 32 are rejected under 103(a) as being unpatentable over Hurpin et al. (1998) Vaccine, Vol. 16, No. 2/3, 208-215 in view of U.S. Patent No. 6,110,744, 8/29/00 (filed on 11/12/97), hereafter referred to as Fang et al, and Reed et al. (1997) Int. J. Cancer, Vol. 72, 1045-1055. The applicant claims methods of treating a hyperproliferative disease in a subject by identifying a subject with a hyperproliferative disease characterized by alteration or increased expression of a self gene product and intradermally administering an expression construct comprising a self tumor suppressor gene under control of a promoter operable in eukaryotic dendritic cells. The applicant further claims said methods wherein the expression construct is an E1 deleted replication-defective adenoviral vector, and wherein the subject is a human.

Hurpin et al., as presented above, teaches that the intradermal injection of a plasmid encoding wild type p53 results in the generation of p53 specific CTL and protection from the growth of a p53 overexpressing mastocytoma (Hurpin et al., page 212, Figure 3, and page 213, Figure 4). Hurpin et al. further teaches that the plasmid encodes p53 under transcriptional control of the CMV immediate-early promoter, and that the plasmid was administered intradermally at five separate sites on the back (Hurpin et al., page 209, column 1, paragraph 3, and column 2,

paragraph 2). Hurpin et al. also teaches that more than 50% of tumors overexpress p53 and further teaches that overexpression of p53 can be determined using well known techniques in molecular biology (Hurpin et al., page 1, column 2, paragraph 2, and page 209).

Hurpin et al. does not teach that the expression vector is an adenoviral vector. Fang et al. supplements Hurpin et al. by teaching an replication defective, E1 deleted, adenovirus which encodes p53 under transcriptional control of the CMV promoter (Fang et al., columns 49-51, claims 1, 7-8, 20-21, and 22-23). Fang et al. further teaches that such replication defective adenoviral vectors with large deletions in adenoviral proteins are particularly preferable for gene therapy and vaccines as the host immune responses to the adenoviral proteins is reduced resulting in prolonged gene expression of the heterologous gene of interest (Fang et al., columns 7, lines 31-44). Reed et al. further provides additional motivation for substituting the adenoviral p53 vector taught by Fang et al. for the plasmid vector taught by Hurpin et al. by teaching that recombinant human viral vectors have many advantages over other viral and non-viral vectors such as high transduction efficiency and ability to produce stable high-titer stocks (Reed et al., page 1045, abstract and column 1). Reed et al. also teaches that cells transduced with an adenoviral vector encoding the melanoma tumor antigen MAGE-1 are recognized are capable of stimulating and being lysed by human CTL (Reed et al., page 1051, Figure 5, and page 1053, Figure 7). In addition, Reed et al. suggests the utility of adenovirus vaccines encoding tumor antigens for treating cancer in human patients (Reed et al., page 1045, abstract).

Thus in view the advantages of using replication defective recombinant adenoviruses for vaccines as taught by Reed et al. and Fang et al., it would have been prima facie obvious to the skilled artisan to substitute the adenoviral p53 vector taught by Fang et al. for the plasmid vector taught by Hurpin et al. in the method of treating cancer taught by Hurpin et al. in order to decrease anti-adenoviral immune responses and increase p53 gene expression. Further, based on the successful use of adenoviral vectors encoding tumor antigens to induce human CTL responses as taught by Reed et al., the skilled artisan would have had a reasonable expectation of success in generating anti-p53 CTL responses in humans using an adenovirus encoding p53 in the method of treating tumors taught by Hurpin et al.

Claims 1 and 34-37 are rejected under 35 U.S.C. 103 as being obvious over Hurpin et al. (1998) Vaccine, Vol. 16, No. 2/3, 208-215 in view of Xiang et al. (1995) Immunity, Vol. 2, 129-135, and further in view of Rosenthal et al. (1994) Blood, Vol. 83(5), 1289-1298. The applicant claims methods of treating a hyperproliferative disease in a subject by identifying a subject with a hyperproliferative disease characterized by alteration or increased expression of a self gene product and intradermally administering an expression construct comprising a self tumor suppressor gene under control of a promoter operable in eukaryotic dendritic cells and a cytokine. The applicant further claims said methods wherein the expression construct encodes said cytokine, or wherein the method comprises the administration of two cytokines.

Hurpin et al., as presented above, teaches that the intradermal injection of a plasmid encoding wild type p53 results in the generation of p53 specific CTL and protection from the growth of a p53 overexpressing mastocytoma (Hurpin et al., page 212, Figure 3, and page 213, Figure 4). Hurpin et al. further teaches that the plasmid encodes p53 under transcriptional control of the CMV immediate-early promoter, and that the plasmid was administered intradermally at five separate sites on the back (Hurpin et al., page 209, column 1, paragraph 3, and column 2, paragraph 2). Hurpin et al. also teaches that more than 50% of tumors overexpress p53 and further teaches that overexpression of p53 can be determined using well known techniques in molecular biology (Hurpin et al., page 1, column 2, paragraph 2, and page 209).

Hurpin et al. does not teach combining a p53 expressing plasmid with a cytokine. Xiang et al. teaches a pharmaceutical composition of two plasmids, one which encodes murine GM-CSF, and the other, rabies virus G protein, and a method of immunizing a mouse against rabies virus by injection of said composition into the mouse prior to challenge with rabies virus (Xiang et al., page 130, Table 1, and column 1). Xiang et al. provides motivation for combining the administration of an antigen with a cytokine such as GM-CSF by teaching that the coadministration of an antigen and GM-CSF enhanced the antiviral immune response (Xiang et al., page 129, abstract). Xiang et al. also provides motivation for using a single plasmid to express both an antigen and a cytokine by teaching that the administration of polycistronic vectors expressing both an antigen and a cytokine may improve the efficacy of DNA vaccines (Xiang et al., page 133, column 2, paragraph 2). Thus based on the motivation provided by Xiang et al., it

would have been *prima facie* obvious to the skilled artisan at the time of filing to include a cytokine expressing plasmid as taught by Xiang et al. in the pharmaceutical composition comprising a p53 expression plasmid taught by Hurpin et al. in order to increase the anti-p53 immune responses *in vivo*. Further, based on the motivation to improve vaccine efficacy by expressing both the antigen and cytokine from one plasmid, it would have been *prima facie* obvious to the artisan to modify the p53 plasmid taught by Hurpin 35 al. to include a cytokine gene linked to a promoter as taught by Xiang et al. using well known techniques of molecular biology.

Neither Hurpin et al. nor Xiang et al. teach the administration of an antigen and two cytokines. Rosenthal et al. supplements Hurpin et al. and Xiang et al. by teaching a retroviral vector that encodes two different cytokines, either IL-2 and IFN-γ , or IL-2 and GM-CSF, and the use of said vector to transduce tumor cells and augment anti-tumor immune responses (Rosenthal et al., page 1289, abstract, and page 1291, Figure 1). Rosenthal et al. also provide motivation for expressing two cytokines from a single vector by teaching that the use of a single vector to carry and express both cytokine genes simplifies gene transfer to cells *in vivo* and ensures simultaneous exposure of effector cells to both cytokines (Rosenthal et al., page 1295, paragraph 1, page 1296, paragraph 3). Thus, based on the motivation provided by Rosenthal et al. to express two cytokines from a single vector, it would have been *prima facie* obvious to the skilled artisan to modify the cytokine encoding plasmid taught by Xiang to include a second

promoter and cytokine gene as taught by Rosenthal using well known techniques of molecular cloning.

Alternatively, in view of the motivation provided by Xiang et al. for using polycistronic vectors to express an antigen and a cytokine gene in order to improve vaccine efficacy, and the motivation provided by Rosenthal et al. to use a single vector to express two cytokine genes, it would have been *prima facie* obvious to the skilled artisan at the time of filing to further modify the plasmid encoding an p53 antigen taught by Hurpin et al. to encode either a single cytokine as taught by Xiang et al., or multiple cytokines as taught by Rosenthal, using well known techniques of molecular biology in order to generate therapeutic anti-p53 immune responses. Further, based on the combined teachings of Hurpin et al. in view of Xiang et al. and Rosenthal et al., the skilled artisan would have had a reasonable expectation of success in generating anti-p53 immune responses and inhibiting p53 positive tumor growth according to the methodology of Hurpin et al. using a single plasmid which encodes an antigen and an immunomodulatory cytokine(s) selected from a group which includes GM-CSF.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02. The oath or declaration is defective because: it does not identify the

post office address of each inventor. A post office address is an address at which an inventor customarily receives his or her mail and may be either a home or business address. The post office address should include the ZIP Code designation.

No claims are allowed.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Beckerleg, Ph.D., whose telephone number is (703) 306-9156. The examiner can be reached Mon-Thurs and every other Friday from 9:30-7:00. General inquiries should be directed to the group receptionist whose phone number is (703) 308-0196. The official fax number is (703) 308-4242.

Dr. A.M.S. Beckerleg

A.M.S. BECKERLEG
PATENT EXAMINER